DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 21-272/S-008

United Therapeutics Corporation
Attention: Kerry McKenzie
P.O. Box 14186
One Park Drive
Research Triangle Park, NC 27709

SUPPLEMENT APPROVAL

Dear Mr. McKenzie:

Please refer to your supplemental new drug application (sNDA) dated October 23, 2007, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Remodulin (treprostinil sodium) Injection 1, 2.5, 5, and 10 mg/mL.

We also refer to your submission dated March 28, 2008.

This supplemental new drug application provides for the following revisions to the package insert:

1. Flolan Sterile Diluent for Injection has been added as an acceptable diluent for intravenous administration to the following sections:
    - DOSAGE AND ADMINISTRATION/General (section 2.1)
    - DOSAGE AND ADMINISTRATION/Administration (section 2.6, under the "Intravenous Infusion" and "Step 2" subheadings).
    - HOW SUPPLIED/STORAGE AND HANDLING (section 16)

2. Under INDICATIONS AND USAGE, section 1.2 has been changed from:

    1.2 Pulmonary Arterial Hypertension In Patients Requiring Transition From Flolan®
    Remodulin is indicated to diminish the rate of clinical deterioration in patients with pulmonary arterial hypertension requiring transition from Flolan (epoprostenol sodium); the risks and benefits of each drug should be carefully considered prior to transition.

    To:

    1.2 Pulmonary Arterial Hypertension In Patients Requiring Transition From Flolan®
    In patients with pulmonary arterial hypertension requiring transition from Flolan (epoprostenol sodium), Remodulin is indicated to diminish the rate of clinical deterioration. The risks and benefits of each drug should be carefully considered prior to transition.

3. Under CLINICAL PHARMACOLOGY, the first paragraph in the Pharmacokinetics section (12.3) has been changed from:

    The pharmacokinetics of continuous subcutaneous Remodulin are linear over the dose range of 1.25 to 22.5 ng/kg/min (corresponding to plasma concentrations of about 0.03 to 8 mcg/L) and can be described by a two-compartment model. Dose proportionality at infusion rates greater than 22.5 ng/kg/min has not been studied.

    To:

    The pharmacokinetics of continuous subcutaneous Remodulin are linear over the dose range of 1.25 to 125 ng/kg/min (corresponding to plasma concentrations of about 15 pg/mL to 18,250 pg/m) and can be described by a two-compartment model. Dose proportionality at infusion rates greater than 125 ng/kg/min has not been studied.

4. The label has been formatted into the new PLR format.

We have completed our review of this application, and it is approved, effective on the date of this letter, for use as recommended in the enclosed labeling text.

As soon as possible, but no later than 14 days from the date of this letter, please submit the content of labeling [21 CFR 314.50(l)] in structured product labeling (SPL) format as described at http://www.fda.gov/oc/datacouncil/spl.html that is identical to the enclosed labeling. Upon receipt, we will transmit that version to the National Library of Medicine for public dissemination. For administrative purposes, please designate this submission, "SPL for approved NDA 21-272/S-008."

If you issue a letter communicating important information about this drug product (i.e., a "Dear Health Care Professional" letter), we request that you submit a copy of the letter to this NDA and a copy to the following address:

MEDWATCH
Food and Drug Administration
Suite 12B05
5600 Fishers Lane
Rockville, MD 20857

We remind you that you must comply with reporting requirements for an approved NDA (21 CFR 314.80 and 314.81).

If you have any questions, call Dan Brum, Pharm.D., Regulatory Project Manager, at (301) 796-0578.

Sincerely,

{See appended electronic signature page}

Norman Stockbridge, M.D., Ph.D.
Director
Division of Cardiovascular and Renal Products
Office of Drug Evaluation I
Center for Drug Evaluation and Research

Enclosure: Labeling Text

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

Norman Stockbridge
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